

Two Phase Thermally Deformable Biocompatible Absorbable
Polymer Matrix for Use in Medical Devices

5

Field of the Invention

10 The general field to which the invention relates to is
devices made of absorbable polymer matrices.
Specifically, absorbable polyester matrices for use in a
thermally deformable plating system for the fixation of
bone and cartilage, especially hard tissue of the
cranium.

15

Background of the Invention

20 Synthetic absorbable biocompatible polymers are well
known in the art. Such polymers are typically used to
manufacture medical devices, which are implanted in body
tissue and absorb over time. Synthetic absorbable
biocompatible polymers include homopolymers, copolymers
(random, block, segmented and graft) of monomers such as
glycolic acid, glycolide (d, l, meso and mixtures
25 thereof), lactic acid, lactide, ϵ -caprolactone,
trimethylene carbonate and p-dioxanone. Numerous U.S.
Patents describe these polymers including 5,431,679;
5,403,347; 5,314,989; 5,431,679; 5,403,347; and
5,502,159.

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There is a constant need in this art for new polymer compositions having improved physical properties when molded or extruded into medical devices and further having excellent in vivo properties. For
5 example, it is known that copolymers of lactide and glycolide have good in vivo properties (U.S. Patent 5,569,250). These materials are also generally known in the art to be single phase, amorphous or semi-crystalline copolymers with melting points exceeding
10 100°C, and no low melting or immiscible component.

Heat deforming of absorbable devices, such as plates, has also been described in U.S. Patent 5,569,250. However, one drawback of such devices is their lack of a
15 visual cue to aid the surgeon in knowing the precise time that they can begin deforming the device. This is critical to the device, because premature bending or otherwise manipulating it before it has relaxed (i.e., heated above its Tg or Tm) can cause stresses to form in
20 the part, weakening it, especially in clinical situations.

Unfortunately, U.S. Patent 5,569,250 does not recognize that absorbable plates, rods and pins, for example,
25 could be manufactured from a polymeric material that provides a visual cue to a surgeon during surgery to assist him/her in appropriately applying the device to the surgical site.

30 Therefore, what is needed in this art is a novel device that provides a visual cue during its application (i.e.,

deformation during heating) to indicate when it can be safely manipulated or shaped.

5 The surgical devices of the present invention provide a visual cue to surgeons indicating when the surgical device may be contoured or shaped.

Summary of the Invention

10 We have discovered an absorbable polymeric matrix that provides a visual cue when heated that the absorbable polymeric matrix may be deformed without significantly reducing the strength (due to internal stress concentration) of a device made from the polymeric
15 matrix. These polymeric matrices are especially well suited for use in implantable surgical devices such as plates, pins, rods and the like that need to be shaped during medical procedures to accommodate the patient. The method of shaping a surgical article containing
20 these absorbable polymeric matrices comprises heating the surgical article until a visual cue is provided by the absorbable polymeric matrix that the portion of the surgical article made from the absorbable polymeric matrix may be safely shaped, then shaping that portion
25 of the surgical article to the desired final shape and allowing the surgical article to cool.

The foregoing and other features and advantages of the invention will become more apparent from the following
30 description and accompanying examples.

Brief Description of the Drawings

Fig. 1 photographically illustrates the visual cue of the device of the present invention. The burr hole cover plate on the left is opaque at room temperature, while the plate on the right has been heated to 55°C is nearly transparent.

Detailed Description of the Invention

10 The biocompatible polymeric materials described herein are matrices having a continuous phase and a disperse phase. The continuous phase is generally composed of an amorphous biocompatible polymeric material. The
15 dispersed phase is composed of a biocompatible material with a low melting point. The dispersed phase is believed to provide scattering centers in the matrix that when heated become transparent. This provides the surgeon a visual cue of when to bend and shape the
20 medical device formed from the matrix. In applications that require shaping the device, such as cranial plating over a variety of bony contours, the present invention is far superior to the devices disclosed in the prior art.

25 The polymeric materials of the present invention are formed of a polymeric matrix with a continuous phase and a dispersed phase of a lower melting crystalline material forming a second distinct phase. The
30 continuous phase is preferably formed from amorphous

biocompatible polymers. Suitable amorphous
biocompatible polymers include, but are not limited to,
amorphous aliphatic ester polymers selected from the
group consisting of amorphous polylactide (including D-
5 lactide, L-lactide, mixtures of D-lactide and L-lactide,
as well as, lactic acid polymers), amorphous
polyglycolide (including polyglycolic acid polymers),
amorphous poly-1,4-dioxan-2-one, amorphous
polytrimethylene carbonate (also known as poly-1,3-
10 dioxan-2-one) and copolymers and blends thereof. For
crystalline compositions the polymers will have a
melting point above 80°C and most preferably above 70°C.

The dispersed phase is a semi-crystalline polymer that
15 will form a separate phase in the continuous matrix and
melt at a temperature between about 40°C to about 65°C,
and most preferably will melt at a temperature in the
range of from about 40°C to about 55°C. Suitable
absorbable biocompatible polymers that may used
20 especially in association with the aliphatic ester
polymers listed for the dispersed phase include, but are
not limited to, biocompatible absorbable polymers
selected from the group consisting of poly(ϵ -
caprolactone); copolymers of ϵ -caprolactone and with up
25 to 40 mole percent of a second monomer selected from the
group consisting of lactide (lactic acid), glycolide
(glycolic acid), 1,4-dioxan-2-one, and trimethylene
carbonate; and copolymers of ϵ -caprolactone or
trimethylene carbonate with greater than 60 mole percent
30 1,4-dioxan-2-one, but less than 90 mole percent.

Additionally, the dispersed phase may be formed from low melting biocompatible organic molecules of an appropriate size to act as scattering sites that may be blended with the matrix without adversely affecting the chemical or mechanical properties of the matrix polymer for its intended use. One suitable organic material is polyethylene glycol (PEG).

Additionally, the continuous phase and the dispersed phase could also be provided by using block copolymers composed of the continuous phase and dispersed phase polymers described above, provided that the block copolymers formed two distinct phases, wherein the dispersed phase block forms scattering sites and the dispersed phase has a melting point in the temperature range previously described.

Generally, the amount of biocompatible material in the dispersed phase will be that amount sufficient to provide a visual cue when the biocompatible materials in the dispersed phase become transparent or melt or otherwise visually changes during heating of the device. By way of a guideline, but not limiting the scope of the present invention, for the combination of the continuous phase aliphatic polyesters previously listed with the dispersed phase biocompatible absorbable polymers previously listed, it is preferred that the weight percent of dispersed polymer comprise in the range of from about 1 to about 50 and most preferable from about 2 to about 20. The weight percentages being based on

the total weight percent of the matrix polymers equaling 100 percent.

5 In a medical procedure the device will be shaped to accommodate the patients individual anatomy or the particular surgical requirements. The medical device would be heated preferably in a liquid media until the medical device provides a visible cue that it may be shaped (without imparting undue stress to the medical
10 device). In one preferred embodiment of the present invention when heated the absorbable polymer matrices under goes a reversible visual change when a substantial amount of the dispersed polymer phase becomes clear by melting. The scattering sites when transparent no
15 longer scatter light and the absorbable polymeric matrix will appear clear as long as the dispersed phase remains above its melting point. For the absorbable polymeric matrix described above the surgeon would heat the matrix to a temperature from about 40°C to about 65°C until it
20 becomes nearly transparent. While the matrix appears clear the surgeon will be able to safely shape the device.

The polymers of the present invention will typically be
25 synthesized in a ring opening polymerization. That is, the aliphatic lactone monomers lactide, glycolide, ϵ -caprolactone, p-dioxanone, and trimethylene carbonate are polymerized in the presence of an organometallic catalyst and an initiator at elevated temperatures. The
30 organometallic catalyst is preferably tin based, e.g.,

stannous octoate, and is present in the monomer mixture at a molar ratio of monomer to catalyst ranging from about 10,000/1 to about 100,000/1. The initiator is typically an alkanol (including diols and polyols), a glycol, a hydroxyacid, or an amine, and is present in the monomer mixture at a molar ratio of monomer to initiator ranging from about 100/1 to about 5000/1. The polymerization is typically carried out at a temperature range from about 80°C to about 240°C, preferably from about 100°C to about 220°C, until the desired molecular weight and viscosity are achieved.

The polymer blends of the present invention are manufactured in a conventional manner, preferably in the following manner. The homopolymers and copolymers, prepared as described above, are individually charged into a conventional mixing vessel or reactor vessel having a conventional mixing device mounted therein, such as an impeller or equivalents thereof. Then, the polymers and copolymers are mixed at a temperature of about 100°C to about 230°C, more preferably from about 160°C to about 200°C, for about 5 to about 90 minutes, more preferably for about 10 to about 45 minutes, until a uniformly dispersed polymer blend is obtained. Then, the polymer blend is further processed by removing it from the mixing device, cooling to room temperature, grinding, and drying under pressures below atmospheric at elevated temperatures for a period of time using conventional apparatuses and processes.

Additionally, a minor amount (less than 5, preferably less than 3 weight percent weight percent) of additional

lactone monomers selected from the group consisting of
1,3-dioxan-2-one, p-dioxanone, delta-valerolactone,
beta-butyrolactone, epsilon-decalactone, 2,5-
diketomorpholine, pivalolactone, alpha, alpha-
5 diethylpropiolactone, ethylene carbonate, ethylene
oxalate, 3-methyl-1,4-dioxane-2,5-dione, 3,3-diethyl-
1,4-dioxan-2,5-dione, gamma-butyrolactone, 1,4-dioxepan-
2-one, 1,5-dioxepan-2-one, 6,6-dimethyl-dioxepan-2-one,
6,8-dioxabicyclooctane-7-one and combinations of two or
10 more thereof may be added.

Under the above described conditions, the polymers and
blends composed of glycolide, epsilon-caprolactone, p-
dioxanone, lactide and trimethylene carbonate will
15 typically have a weight average molecular weight of
about 20,000 grams per mole to about 300,000 grams per
mole, more typically about 40,000 grams per mole to
about 200,000 grams per mole, and preferably about
60,000 grams per mole to about 150,000 grams per mole.
20 These molecular weights provide an inherent viscosity
between about 0.5 to about 4.0 deciliters per gram
(dL/g), more typically about 0.7 to about 3.5 dL/g, and
most preferably about 1.0 to about 3.0 dL/g as measured
in a 0.1 g/dL solution of hexafluoroisopropanol (HFIP)
25 at 25°C. Also, it should be noted that under the above
described conditions, the residual monomer content would
be less than about 5 weight percent.

Articles such as medical devices are molded from the
30 polymers and blends of the present invention by use of
various injection and extrusion molding equipment

equipped with dry nitrogen atmospheric chamber(s) at temperatures ranging from about 100°C to about 230°C, more preferably 140°C to about 200°C, with residence times of about 1 to about 20 minutes, more preferably
5 about 2 to about 10 minutes.

The polymers and blends of the present invention can be melt processed by numerous methods to prepare a vast array of useful devices. These materials can be
10 injection or compression molded to make implantable medical and surgical devices, including wound closure devices. The preferred devices are orthopedic plates, pins and rods.

15 Alternatively, the blends and polymers can be extruded to prepare fibers. The materials of the present invention may also be spun as multifilament yarn and woven or knitted to form sponges or gauze, (or non-woven sheets may be prepared) or used in conjunction with
20 other molded compressive structures such as prosthetic devices within the body of a human or animal where it is desirable that the structure have high tensile strength and desirable levels of compliance and/or ductility. Useful embodiments include tubes, including branched
25 tubes, for artery, vein or intestinal repair, nerve splicing, tendon splicing, sheets for tying up and supporting damaged surface abrasions, particularly major abrasions, or areas where the skin and underlying tissues are damaged or surgically removed.

30

Additionally, the polymers and blends can be molded to form films which, when sterilized, are useful as adhesion prevention barriers.

- 5 In another embodiment of the present invention, the polymers and blends can be used as a drug delivery matrix. To form this matrix, the polymer would be mixed with a therapeutic agent. The variety of different therapeutic agents that can be used in conjunction with the polymers of the present invention is vast. In general, therapeutic agents which may be administered via the pharmaceutical compositions of the invention include, without limitation:
- 10 antiinfectives such as antibiotics and antiviral agents; analgesics and analgesic combinations; anorexics; antihelminthics; antiarthritics; antiasthmatic agents; anticonvulsants; antidepressants; antidiuretic agents; antidiarrheals; antihistamines; antiinflammatory agents; antimigraine preparations; antinauseants; antineoplastics; antiparkinsonism drugs; antipruritics; antipsychotics;
- 15 antipyretics, antispasmodics; anticholinergics; sympathomimetics; xanthine derivatives; cardiovascular preparations including calcium channel blockers and beta-blockers such as pindolol and antiarrhythmics; antihypertensives; diuretics; vasodilators including
- 20 general coronary, peripheral and cerebral; central nervous system stimulants; cough and cold preparations, including decongestants; hormones such as estradiol and other steroids, including corticosteroids; hypnotics; immunosuppressives; muscle relaxants; parasympatholytics;
- 25 psychostimulants; sedatives; and tranquilizers; and
- 30

naturally derived or genetically engineered proteins, polysaccharides, glycoproteins, or lipoproteins.

5 The drug delivery matrix may be administered orally, parenterally, subcutaneously, vaginally or anally. Matrix formulations may be formulated by mixing one or more therapeutic agents with the polymer. The therapeutic agent, may be present as a liquid, a finely divided solid, or any other appropriate physical form. Typically, but
10 optionally, the matrix will include one or more additives, such as diluents, carriers, excipients, stabilizers or the like.

15 The amount of therapeutic agent will depend on the particular drug being employed and medical condition being treated. Typically, the amount of drug represents about 0.001% to about 70%, more typically about 0.001% to about 50%, most typically about 0.001% to about 20% by weight of the matrix.

20 The quantity and type of polymer incorporated into the drug delivery matrix will vary depending on the release profile desired and the amount of drug employed.

25 Upon contact with body fluids, the polymer undergoes gradual degradation (mainly through hydrolysis) with concomitant release of the dispersed drug for a sustained or extended period. This can result in prolonged delivery (over, say 1 to 5,000 hours, preferably 2 to 800 hours) of
30 effective amounts (say, 0.0001 mg/kg/hour to 10 mg/kg/hour) of the drug. This dosage form can be

administered as is necessary depending on the subject being treated, the severity of the affliction, the judgment of the prescribing physician, and the like.

- 5 Following this or similar procedures, those skilled in the art will be able to prepare a variety of formulations.

Furthermore, the polymers and blends of the present invention can be processed by conventional techniques to
10 form foams, which are useful as hemostatic barriers, bone substitutes, and tissue scaffolds.

In more detail, the surgical and medical uses of the filaments, films, foams and molded articles of the
15 present invention include, but are not necessarily limited to knitted products, woven or non-woven, and molded products including:

- a. burn dressings
- 20 b. hernia patches
- c. medicated dressings
- d. fascial substitutes
- e. gauze, fabric, sheet, felt or sponge for liver hemostasis
- 25 f. gauze bandages
- g. arterial graft or substitutes
- h. bandages for skin surfaces
- i. burn dressings
- j. bone substitutes
- 30 k. needles
- l. intrauterine devices

- m. draining or testing tubes or capillaries
- n. surgical instruments
- o. vascular implants or supports
- p. vertebral discs
- 5 q. extracorporeal tubing for kidney and heart-lung machines
- r. artificial skin and others
- s. stents
- t. suture anchors
- 10 u. injectable defect fillers
- v. preformed defect fillers
- w. tissue adhesives and sealants
- x. bone waxes
- y. cartilage replacements
- 15 z. hemostatic barriers
- aa. tissue scaffolds
- bb. monofilament and braided sutures
- cc. orthopedic, spinal and nuerosurgical plates, rods and pins.

20

The following non-limiting examples are illustrative of the principles and practice of this invention. Numerous additional embodiments within the scope and spirit of the invention will become apparent to those skilled in
25 the art.

Examples

The examples describe an opaque plating system that
30 comprises a polymer or polymer blends that when heated

is transparent then opaque again upon cooling to body temperature.

5 In the synthetic process, the high molecular weight aliphatic polyesters are prepared by a method consisting of reacting lactone monomers via a ring opening polymerization at temperatures of 100°C to 230°C for 2 to 24 hours under an inert nitrogen atmosphere until the desired molecular weight and viscosity are achieved.

10

In the blending process, the polymer blends of the present invention are prepared by individually charging the synthesized aliphatic homo- and co-polyesters into a conventional mixing vessel. The homopolymers and copolymers
15 are mixed at a temperature of 100°C to 230°C, for 5 to 90 minutes until a uniformly dispersed polymer blend is obtained.

In the examples which follow, the blends, polymers and
20 monomers were characterized for chemical composition and purity (NMR, FT-IR), thermal analysis (DSC), melt rheology (melt stability and viscosity), molecular weight (inherent viscosity), and baseline mechanical properties (Instron stress/strain).

25

Inherent viscosities (I.V., dL/g) of the blends and polymers were measured using a 50 bore Cannon-Ubbelohde dilution viscometer immersed in a thermostatically controlled water bath at 25°C utilizing chloroform or
30 HFIP (hexafluoroisopropanol) as the solvent at a concentration of 0.1 g/dL.

Several examples will be described in the following few pages. Parts and percentages where used are parts and percentages as specified as weight or moles.

5

EXAMPLE 1

Synthesis of a 85:15 (mol/mol) poly(lactide-co-glycolide) copolymer

10

The method described below and utilized in this example is similar to those described in U.S. Patent Nos. 4,643,191, 4,653,497, 5,007,923, 5,047,048 which are incorporated by reference, and is known to those skilled in the art.

15

To a flame dried 500 mL 1-neck round bottom flask equipped with an overhead mechanical stirrer and nitrogen inlet, 268 grams (1.86 moles) of L(-) lactide, 38.4 grams (0.330 moles) of glycolide, 0.53 grams (7×10^{-3} moles) of glycolic acid initiator, and 131 microliters of a 0.33 M solution of stannous octoate catalyst were added.

20

The assembly was then placed in a high temperature oil bath at 185°C. The stirred monomers quickly began to melt. The low viscosity melt quickly increased in viscosity. Mechanical stirring of the high viscosity melt was continued for a total reaction time of 4 hours.

25

The 85:15 (mol/mol) poly(lactide-co-glycolide) copolymer was removed from the bath, cooled to room temperature under a

30

stream of nitrogen, isolated and ground. The polymer was then dried under vacuum at 110°C for 24 hours. Inherent viscosity using HFIP as a solvent was 1.90 dL/g.

5 EXAMPLE 2

Synthesis of a 95:5 (mol/mol) poly(ϵ -caprolactone-co-p-dioxanone) copolymer

- 10 The method described below in this example is similar to those described in U.S. Patent Nos. 4,643,191, 4,653,497, 5,007,923, 5,047,048 which are incorporated by reference, and is known to those skilled in the art.
- 15 To a flame dried 500 mL 1-neck round bottom flask equipped with an overhead mechanical stirrer and nitrogen inlet, 262.43 grams (2.3 moles) of ϵ -caprolactone, 12.38 grams (0.12 moles) of p-dioxanone, 0.84 grams (0.011 moles) of glycolic acid initiator, and 147 microliters of a 0.33 M
- 20 solution of stannous octoate catalyst were added.

- The assembly was then placed in a high temperature oil bath at 190°C. The stirred monomers quickly began to melt. The low viscosity melt quickly increased in viscosity. Mechanical
- 25 stirring of the high viscosity melt was continued for a total reaction time of 24 hours.

- The 95:5 (mol/mol) poly(ϵ -caprolactone-co-p-dioxanone) copolymer was removed from the bath, cooled to room
- 30 temperature under a stream of nitrogen, isolated and ground.

The polymer was then dried under vacuum at 40°C for 24 hours. Inherent viscosity using HFIP as a solvent was 1.77 dL/g.

EXAMPLE 3

5 Blending of a 85:15 (mol/mol) poly(lactide-co-glycolide) copolymer with a 95:5 (mol/mol) poly(ϵ -caprolactone-co-p-dioxanone) copolymer at a blended weight ratio of 95:5

10 29.45 grams of a 85:15 (mol/mol) poly(lactide-co-glycolide) prepared as described in Example 1 was melt blended with 1.55 grams of the 95:5 (mol/mol) poly(ϵ -caprolactone-co-p-dioxanone) copolymer of Example 2 at a weight ratio of 95:5 in a Brabender Plasti-corder mixer

15 at a temperature of 170°C for 23 minutes. The resulting blend was removed from the Brabender mixer, cooled, ground and dried under vacuum at 50°C for 24 hours. Inherent viscosity using HFIP as a solvent was 1.90 dL/g.

20

EXAMPLE 4

Blending of a 85:15 (mol/mol) poly(lactide-co-glycolide) copolymer with a 95:5 (mol/mol) poly(ϵ -caprolactone-co-p-dioxanone) copolymer at a blended weight ratio of 80:20

25

24.8 grams of a 85:15 (mol/mol) poly(lactide-co-glycolide) prepared as described in Example 1 was melt blended with 6.2 grams of the 95:5 (mol/mol) poly(ϵ -caprolactone-co-p-dioxanone) copolymer of Example 2 at a

30

weight ratio of 80:20 in a Brabender Plasti-corder mixer at a temperature of 170°C for 23 minutes. The resulting blend was removed from the Brabender mixer, cooled, ground and dried under vacuum at 50°C for 24 hours.

- 5 Inherent viscosity using HFIP as a solvent was 1.83 dL/g.

EXAMPLE 5

- 10 Blending of a 85:15 (mol/mol) poly(lactide-co-glycolide) copolymer with a 95:5 (mol/mol) poly(ε-caprolactone-co-p-dioxanone) copolymer at a blended weight ratio of 60:40

- 15 18.6 grams of a 85:15 (mol/mol) poly(lactide-co-glycolide) prepared as described in Example 1 was melt blended with 12.4 grams of the 95:5 (mol/mol) poly(ε-caprolactone-co-p-dioxanone) copolymer of Example 2 at a weight ratio of 60:40 in a Brabender Plasti-corder mixer at a temperature of 170°C for 23 minutes. The resulting
20 blend was removed from the Brabender mixer, cooled, ground and dried under vacuum at 50°C for 24 hours. Inherent viscosity using HFIP as a solvent was 1.80 dL/g.

EXAMPLE 6

Synthesis of a 60:40 (mol/mol) poly(ϵ -caprolactone-co-L-lactide) copolymer

- 5 The method described below in this example is similar to those described in U.S. Patent Nos. 4,643,191, 4,653,497, 5,007,923, 5,047,048 which are incorporated by reference, and is known to those skilled in the art.
- 10 To a flame dried 500 mL 1-neck round bottom flask equipped with an overhead mechanical stirrer and nitrogen inlet, 165.75 grams (1.45 moles) of ϵ -caprolactone, 139.68 grams (0.97 moles) of L-lactide, 0.84 grams (0.011 moles) of glycolic acid initiator, and 147 microliters of a 0.33 M
- 15 solution of stannous octoate catalyst are added.

The assembly is then placed in a high temperature oil bath at 190°C. The stirred monomers quickly began to melt. The low viscosity melt quickly increased in viscosity. Mechanical

20 stirring of the high viscosity melt is continued for a total reaction time of 24 hours.

The 60:40 (mol/mol) poly(ϵ -caprolactone-co-L-lactide) copolymer is removed from the bath, cooled to room

25 temperature under a stream of nitrogen, isolated and ground. The polymer is then dried under vacuum at 40°C for 24 hours. Inherent viscosity using HFIP as a solvent is 1.92 dL/g.

EXAMPLE 7

Injection molding a circular plate (of Fig. 1) of a blend of
85:15 poly(lactide-co-glycolide) copolymer and 95:5 poly(ϵ -
5 caprolactone-co-p-dioxanone) copolymer at a blended weight
ratio of 95:5

1.5 Kg of a blend as formed in Example 3 was added to a
nitrogen purged hopper of a 28 ton Engel injection molder
10 equipped with an 18 mm diameter barrel to form a circular
plate as shown in Fig.1. Three heating zones of 180, 170,
and 140°C were employed to melt the blend as it entered the
barrel. A nozzle temperature of 185°C with an injection
pressure of 700 psi and a speed of 2 in/s were used to feed
15 the molten material down the barrel. Each injection produced
a single part in a single cavity mold. A temperature of 45°C
was used in the mold to optimize the stress levels in the
part. Using this process 2 parts are formed per minute.

20

EXAMPLE 8

A circular burr hole cover plate (as illustrated in Figure
1) was manufactured from the matrix described in Example 3
25 by the injection molding process described in Example 7.
The plate was then immersed in a vessel containing a
biocompatible heat transfer medium (i.e. warm water, . . .)
at a temperature of about 50-60°C, until the plate became
clear. This visual cue signals the surgeon that the plate
30 may be removed from the vessel and shaped by bending it
without causing damage to the plate. The surgeon would then

- 22 -

secure the plate to a fracture site in a conventional manner using conventional fasteners (i.e. rivets, pins and screws).